REMARKS

Claims 70 and 71 are added herein. Claims 11, 23, 34, 35 and 58 are amended herein. Support for new claim 70 can be found in the specification at page 34, lines 16-17. Support for new claim 71 can be found in the specification at page 18, lines 5-12. Support for the amendment of claim 35 can be found in claim 34. Support for the amendment of claim 58 can be found in the specification at FIG. 2. Following entry of this amendment, claims 1, 2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34, 35, 38, 40, 41, 48-71 are pending.

No new matter is added by any of the foregoing amendments. Reconsideration of the subject application is respectfully requested.

Supplemental Information Disclosure Statement (IDS)

Applicants note that the Office action, dated December 3, 2003, does not indicate that the Supplemental IDS, filed on May 12, 2003, has been considered. For the Examiner's convenience, attached is an additional copy of the IDS and the form PTO-1449 (Exhibit A) submitted on May 12, 2003. Also attached is a copy of the postcard documenting receipt by the PTO on May 14, 2003 (Exhibit B). Applicants respectfully request that the Examiner consider this IDS and initial and date the form PTO-1449, and return it to the undersigned.

Withdrawal of Rejections

Applicants thank the Examiner for withdrawing the rejection of claims 10, 34, 35, 53, 57, and 69 under 35 U.S.C. §112, second paragraph. Applicants also thank the Examiner for

withdrawing the rejection of claims 1, 2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34-35, 38, 40, 41, 48, 49, 51-55, and 66-69 under 35 U.S.C. §112, first paragraph.

Claim objections

Claim 35 is objected to as allegedly depending from a rejected claim. Applicants have amended claim 35 to make it an independent claim. Applicants submit that the amendment removes the objection. Reconsideration and withdrawal of the objection are respectfully requested.

Rejections Under 35 U.S.C. §112, second paragraph

Claim 58 is rejected as allegedly being indefinite because it is not clear if the murine residues that are replaced at positions 60, 61, 62, or 64 are those at positions 12, 13, 14, or 16 in SEQ ID NO: 11 or if residues 12, 13, 14, or 16 are additionally human residues in addition to 60, 61, 62, or 64. Applicants respectfully disagree with the rejection. However, in order to advance prosecution in this case, Applicants amend claim 58 to recite "wherein the amino acid at position 60 is a serine, the amino acid at position 61 is a glutamine, the amino acid at position 62 is a lysine, or the amino acid at position 64 is a glutamine." Applicants note that this amendment just specifies the enumerated amino acids shown in SEQ ID NO: 11. Applicants submit that this amendment removes the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejections Under 35 U.S.C. §103

Claims 1, 2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34, 38, 40, 41, 48-69 are rejected as allegedly being obvious over Mezes *et al.*, (U.S. Patent Number 6,495,137), in light of Padlan *et al.*, (*FASEB J.*, 9:133-139, 1995), as evidenced by Tamura *et al.* (*J. Immunol.*, 164:1432-41, 2000). Applicants respectfully disagree with this assertion.

The pending claims are directed to humanized anti-TAG-72 CC49 antibody variants, with *reduced immunogenicity* and *retained antigen binding affinity*, that contain either human LEN L-CDR1, LEN L-CDR2, or both. The specification describes that these CC49 variants were generated by substituting the entire *murine* CC49 L-CDR1, L-CDR2, or both, with the corresponding *human* LEN L-CDR. Prior to generating such variants, *each murine CC49 CDR residue must be evaluated* in order to determine if the *murine* residue is important for antigen binding, thereby determining whether it can be substituted.

Table 2 of Padlan *et al.* teaches that only one position (27f) in the *murine* L-CDR1 may be important in antigen binding. Based on the information provided by Table 2, one of skill in the art would expect that making a substitution at position 27(f) or making a substitution of the entire murine CC49 L-CDR1 would result in a *decrease* in antigen binding affinity. Thus, Padlan *et al.* teaches away from i) making a substitution of the murine residue at position 27(f) or ii) from substituting the entire murine L-CDR1, when generating a humanized CC49 variant that retains antigen binding affinity. It is only the inventors' own work (for example, see page 28, lines 9-14) that teaches that position 27(f) is not directly involved in antigen contact and that the residue at position 27(f) can be substituted, without compromising antigen binding affinity.

Mezes *et al.* teaches that there is high homology between LEN and CC49 and that the LEN light chain residues can be used for the humanization of the murine monoclonal CC49 antibody. However, Mezes *et al.* does not teach that murine residue 27(f), specifically, can be substituted. Therefore, Mezes *et al.* does not overcome the shortcomings of Padlan *et al.* Thus, it would not be obvious, based on the teachings of Padlan *et al.* and Mezes *et al.* to substitute the entire murine L-CDR1, including the residue at position 27(f), in order to generate a humanized CC49 antibody having both reduced immunogenicity *and* retained antigen binding affinity. Applicants respectfully wish to point out that the information in Table 4 of Padlan *et al.* refers to possible antigen binding positions within *human* L-CDRs. Thus, Table 4 is not relevant to this discussion.

Similarly, Table 2 of Padlan *et al.* teaches that positions 50, 53 and 55 in the *murine* L-CDR2 may be important for antigen binding. Thus, Padlan *et al.* teaches away from i) making a substitution of the murine residue either at position 50, 53, or 55 or ii) from substituting the entire murine L-CDR2, when generating a humanized CC49 variant that retains antigen binding affinity.

The CC49 residues at positions 50 and 55 of L-CDR2 are the same as those at the corresponding positions in the LEN L-CDR2. However, the residue at position 53 differs between CC49 and LEN. Based on the information provided by Table 2, one of skill in the art would expect that substituting the residue at position 53 of the murine CC49 L-CDR2 with the residue at the corresponding position of the human LEN L-CDR2, or making a substitution of the

entire murine CC49 L-CDR2 with the human LEN L-CDR2, would result in a *decrease* in antigen binding affinity. However, Applicants' specification teaches that a murine-to-human substitution at position 53 in L-CDR2 does not affect antigen binding (for example, see the specification at page 25, line 7). This result could not have been predicted from the information provided in Table 2 of Padlan *et al.*

Mezes *et al.* does not teach that an amino acid substitution can be tolerated at L-CDR2 position 53, specifically. Therefore, Mezes *et al.* does not overcome the shortcomings of Padlan *et al.* Thus, it would not be obvious, based on the teachings of Padlan *et al.* and Mezes *et al.* to substitute the entire murine L-CDR2, including the residue at position 53, in order to generate a humanized CC49 antibody having reduced immunogenicity, without compromising antigen binding affinity. Applicants respectfully wish to point out that the information in Table 4 of Padlan *et al.* refers to possible antigen binding positions within *human* L-CDRs. Thus, Table 4 is not relevant to this discussion.

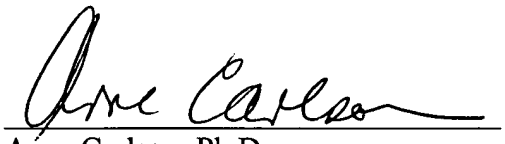
All of the pending claims are directed to humanized CC49 variants having a human LEN L-CDR1, L-CDR2 or both. Consequently, Applicants submit that, based on the above discussion, pending claims 1, 2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34, 38, 40, 41, 48-69 are not obvious in light of Padlan *et al.*, or Mezes *et al.*, alone or in combination. Reconsideration and withdrawal of the rejection with regards to these claims is respectfully requested.

CONCLUSIONS

Based on the foregoing, the claims are in condition for allowance and notification to this effect is requested. If for any reason the Examiner believes that a telephone conference would expedite allowance of the claims, please telephone Applicants' undersigned representative at (503) 226-7391.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 

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